administering to the animal an effective amount of the compound of claim 81 to stimulate growth of damaged peripheral nerves or to promote neuronal regeneration.

84. The method of claim 83, wherein the compound is non-immunosuppressive.

85. The method of claim 83, wherein the neurological disorder is selected from the group consisting of peripheral neuropathies caused by physical injury or disease state, physical damage to the brain, physical damage to the spinal cord, stroke associated with brain damage, and neurological disorders relating to neurodegeneration.

86. The method of claim 83, wherein the neurological disorder is selected from the group consisting of Alzheimer's Disease, Parkinson's Disease, and amyotrophic lateral sclerosis.

87. The method of claim 83, wherein the neurological disorder is Alzheimer's Disease.

88. The method of claim 83, wherein the neurological disorder is Parkinson's Disease.

89. The method of claim 83, wherein the neurological disorder is amyotrophic lateral sclerosis.

REMARKS

Claims 3-8, 11, 14-27, and 72-89 are pending in the present application. The claims have been amended in the expectation that

the amendments will place this application in condition for allowance. The majority of the amendments have been made to remove non-elected subject matter and to narrow the scope of the claims. The amendments do not introduce new matter within the meaning of 35 U.S.C. § 132. Accordingly, entry of the amendments is respectfully requested.

1. Interview Summary

Applicants would like to thank the Examiner for the interview conducted on June 12, 2000. During the interview, the Examiner and applicants discussed the references of record and possible claim amendments or additional submissions to remove the applicability of the cited references.

2. Restriction/Election Requirement

The Official Action states that the Restriction/Election requirement has been finalized for the following reasons:

> Applicant's election with traverse of Group I in Paper No. 11, dated Oct. 21, 1999 is acknowledged. The traversal is on the ground(s) that there is no extra burden to search all the claims. This is not found persuasive because the reason for restriction is that the claims are drawn to independent and patentably distinct compounds which differ in elements, bonding arrangements and chemical properties to such an extend that a reference anticipates a compound would not render another compound in the same obvious.
> According to MPEP 803.02 restriction for Markush claims, broadly, unity of invention exists where compounds included within a Markush group (I) share a common utility **and** (ii) share a substantial structural feature disclosed as being essential to that utility. From the above evidenced provided by applicants proviso out from the

claims, no common core essential to the claimed utility can be found for the Markush claims.
It is noted that the compounds being proviso out at the end of claim 1 and the structural delineation submitted with the PTO-1449 have structural diversified rings for independent and distinct uses e.g.:
CA 95:88473, n=1, D is bond, R2 is CON-OH, as antiinflammatory agent;
CA 130:24972, n=2, D is bond, R2 is CON-OH, as metalloproteinase inhibitor.
It is further evidenced that not only the different size rings are structural material for distinct utility, but also the 2-substituents i.e. the different species being drawn to the different structure are patentably distinct and independent. In the event that applicant's traversal is also on the ground that the species are not patentably distinct, applicant did not submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.
If such identification or admission were made, then there could have been no patentability of all the inventions over Aketa et al. CA 85:1080,839 since RN 60369-21-3 anticipates the claims (please note that these are examples of the patentably distinct variations for R2 by sample search).
The requirement is still deemed proper and is therefore made FINAL.
Based on the election, the subject matter being examined are those compounds of claims 1-11 wherein n=1, R2 is CN or a bioisostere thereof.
Applicants did not elect a specific disease/pathology to be prosecuted with the elected species (incomplete response). Claims 14-25 are included in the examination to the scope of claim 16 and to the extend of the elected compounds. Claims 12-13 and 26-71 are withdrawn from consideration per 37 CFR 1.142(b).

Applicants have amended the claims so that they are now directed solely to elected subject matter. Non-elected subject matter has been removed from the claims without any prejudice or

disclaimer to the removed subject matter.

Regarding the specific disease/pathology to be prosecuted with the elected species, applicants respectfully request reconsideration of this requirement. A search and examination of all the claimed diseases/pathologies would not impose a serious burden on the Examiner. Each of the claimed diseases/pathologies are directed to methods of treating nerves and are accordingly significantly related to each other. If a search and examination of an entire application can be made without serious burden, the Examiner must examine it on the merits. MPEP § 803.

However, to be considered responsive to the election requirement, Applicants provisionally elect Parkinson's Disease as the specific disease/pathology to be treated. The Examiner is reminded that upon election of a species, the Examiner must broaden her search if no art against the elected invention is uncovered.

Regarding the 2-substituents of the present invention, all of these compounds have a common core of being carboxylic acids or carboxylic acid isosteres. The different species embodied in the claimed genus' are not obvious variants of each other since they all represent part of the same inventive concept.

3. Submitted References

The Official Action states that submitted references have been reviewed as follows:

> An enormous number of prior art references have been submitted without description of relevancy. These references as cited on the 1449 have been given a **cursory** review commensurate to the manner they ar submitted.

Applicants would like to point out to the Examiner that a Letter to the Examiner was filed on December 30, 1999 describing the particular relevancy of the cited references, a copy of which is included for the Examiner's convenience.

4. Rejection of Claims 1-2 under 35 U.S.C. § 102(b)

The Official Action states that claims 1-2 are rejected under 35 U.S.C. § 102(b) as being anticipated by Busson et al.

As the basis of this rejection, the Official Action states:

> Claims 1-2 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Busson et al. CA 89:215152. See RN 67488-67-9 delineated.

Claims 1 and 2 have been canceled, removing the present grounds for rejection.

5. Rejection of Claims 1-2 under 35 U.S.C. § 102(b)

The Official Action states that claims 1-2 are rejected under 35 U.S.C. § 102(b) as being anticipated by JP 55-153763.

As the basis of this rejection, the Official Action states:

> Claims 1-2 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by JP 55-153763 (cited on 1449). See p. 3, right column, compound #36.

Claims 1 and 2 have been canceled, removing the present grounds for rejection.

6. Rejection of Claims 1-11 and 14-25 under 35 U.S.C. § 103(a)

The Official Action states that claims 1-11 and 14-25 are rejected under 35 U.S.C. § 103(a) as being obvious over CA 89:215152 (Busson et al.).

As the basis of this rejection, the Official Action states:

> Claims 1-11, 14-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over CA 89:215152.
> The difference between the elected species and the Busson et al. is that the reference has a D is methylene chain while the elected compound has a different chain length. Variation in chain length is normally a skill within the chemical art for compound preparation in absence of unexpected results. In re Lohr 137 USPQ 548; in re Hoke 195 USPQ 148.

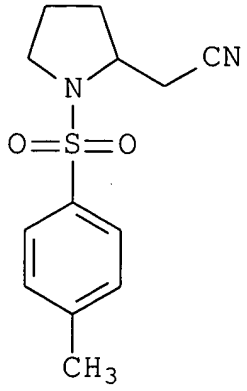
Applicants respectfully traverse this rejection. The reference of record does not teach or suggest applicants' inventive subject matter as a whole as recited in the claims.

Claims 1-2 and 9-10 have been canceled, removing the present grounds for rejection as it applies to these claims.

Claims 6-8 and 11 claim pharmaceutical compositions. The cited reference does not in any way teach or suggest the use of the embodied compounds in pharmaceutical compositions. Accordingly, these claims are unobvious over the cited reference.

Claims 14-25 claim methods of treating neurological disorders in an animal. The cited reference does not in any way teach or suggest treating neurological disorders. Accordingly, these claims are unobvious over the cited reference.

Busson et al. (J. Org. Chem., Vol. 43, No. 23, pp. 4438-4441 (1978)), discloses the following compound:



as an intermediate to arrive at a carbon analogue of penicillin.

The compound has a cyano-substituted methyl group attached at the 2-position of the central pyrrolidine ring. The cyano moiety does not fall within the genus of claim 3. Further, this compound is specifically provisoed out of the genus of claim 4, i.e. "further provided that: when D is methyl, and R_2 is cyano or COOH, then R_1 is not substituted phenyl". This compound is not specifically recited among the species claimed in claim 5.

The compound of Busson et al. is disclosed as an intermediate only. The compound is not disclosed as having any utility as a neurotrophic agent. Busson et al. do not suggest that any of the embodied compounds are useful for regrowing nerves. Since the disclosed compounds are intermediates, a person of ordinary skill in the art would not have expected these compounds to be neurotrophic agents.

Accordingly, the Examiner has provided no motivation to one of ordinary skill in the art to modify Busson et al. to arrive at the presently claimed compounds. Compound claims 3-5 are unobvious over the cited reference.

Accordingly, applicants respectfully request the Examiner to reconsider and withdraw the rejection of remaining claims 3-8, 11, and 14-25.

6. Rejection of Claims 1-11 and 14-25 under 35 U.S.C. § 103(a)

The Official Action states that claims 1-11 and 14-25 are rejected under 35 U.S.C. § 103(a) as being unpatentable over JP 55-215152; CA 118:80750; or WO 92/21313 in view of Andersen et al.

As the basis of this rejection, the Official Action states:

> Claims 1-11, 14-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP 55-215152; CA 118:80750 (1449) or WO 92/21313 in view of Anderson et al. CA 125:104525. The JP 55-215152; CA 118:80750 (1449) or WO 92/21313 references disclosed the isostere ester with or without a linker between the ester moiety and the pyrrolidinyl ring. The difference between the claims and the references is that instead of ester, the elected species is drawn to R2 is cyano. The nitrile moiety is conventional isostere for the ester or amide carboxylic isostere as taught by Anderson.
> One having ordinary skill in the art is well informed of the interchangeability between the various carboxylic isosteres and would be motivated to replace one with another with the expectation that such isosteres would have similar functionality.

Applicants respectfully traverse this rejection. The references of record do not teach or suggest Applicants' inventive subject matter as a whole as recited in the claims.

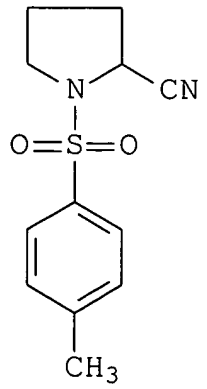
A. JP 55-215152

The Examiner has failed to provide applicants with a copy of the presently cited reference, JP 55-215152. Under MPEP § 707.05(a), copies of cited references should automatically be furnished to applicants together with the Office Action in which they are cited. Copies of foreign patent documents and nonpatent literature (NPL) which are cited by the Examiner are specifically required to be furnished to applicants with the Office Action. The Examiner has a duty to provide applicants with copies of the cited references.

Applicants did not cite the present reference, JP 55-215152, in any of the submitted Information Disclosure Statements. Additionally, applicants have neither been able to obtain a copy of the cited references through a commercial document provider nor been able to even verify the existence of this document using several on-line databases. This is not a valid reference against the present application. Accordingly, the claims of the present invention are unobvious over the cited reference.

B. Ahman et al., CA 118:80750

Ahman et al. (Tetrahedron, Vol. 48, No. 43, pp. 9537-9544 (1992)) disclose the following compound:



as an intermediate. Ahman et al. also disclose similar compounds having either a hydroxy or a methoxy group attached at the 2-position of the central pyrrolidine ring instead of the cyano group as intermediates. No use is disclosed for the final products.

The cyano, hydroxy, and methoxy moieties do not fall within the genus of claim 3. Further, these compounds are specifically provisoed out of the genus of claim 4, i.e. "further provided that: when D is a bond and R_2 is cyano, then R_1 is not 4-methylphenyl" and "further provided that: when D is a bond, and R_2 is hydroxy, alkoxy,..., then R_1 is not...substituted or unsubstituted phenyl". These compounds are not specifically recited among the species claimed in claim 5. Accordingly, compound claims 3-5 are unobvious over the cited reference.

The compounds of Ahman et al. are disclosed as intermediates only. Neither the compounds nor their final product are disclosed as having any utility as a neurotrophic agent. Ahman et al. do not suggest that any of the embodied compounds are useful for regrowing

nerves. The reference provides no expectation to a person of ordinary skill in the art that these compounds could be used as neurotrophic agents.

Additionally, Ahman et al. disclose a compound having an ethyl ester attached by a methyl at the 2-position of the central pyrrolidine ring and an N-linked sulfonamide. An ester group is not included among the specific carboxylic acid isosteres recited in the presently claimed invention.

Andersen et al. do not remedy these deficiencies. Andersen et al. (J. Med. Chem., 31, 417-425 (1996)) state that it is possible to convert a carboxamide group "into acid derivatives such as carboxylic esters and carbonitriles". Additionally, the Examiner cites Andersen et al. to show that "the nitrile moiety is conventional isostere for the ester or amide carboxylic isostere". However, it would not have been obvious to a person of ordinary skill in the art at the time the invention was made to substitute the ester of Duffy with a carboxylic acid or a carboxylic acid isostere such as the nitrile moiety.

The mere possibility that an ester could be modified or replaced to arrive at a different compound would not be obvious "unless the prior art suggested the desirability of [such] a modification or replacement." *In re Brouwer*, 37 U.S.P.Q.2d 1663, 1666 (Fed. Cir. 1996); *In re Gordon*, 221 U.S.P.Q. 1125, 1127 (Fed.

Cir. 1984). Nothing in the prior art suggested the desirability of replacing an ester group with a carboxylic acid or carboxylic acid isostere to arrive at the present inventive compounds.

Additionally, 35 U.S.C. § 103 requires a "fact-intensive comparison of the claimed process with the prior art rather than the mechanical application of one or another *per se* rule." *In re Ochiai*, 37 U.S.P.Q.2d 1127, 1132 (Fed. Cir. 1995). The use of *per se* rules flouts section 103 and the fundamental case law applying it. *Per se* rules that eliminate the need for fact-specific analysis of claims and prior art are legally incorrect and must cease. *Id.* at 1133. Accordingly, the Examiner's position that the present carboxylic acids and carboxylic acid isosteres are *per se* obvious over the prior art references of record showing ester compounds is incorrect. Rather, a fact based inquiry of obviousness is appropriate. Under this inquiry, it is clear that it would not have been obvious to a person of ordinary skill in the art to modify the teachings of Ahman et al. to arrive at the presently claimed invention. The claimed invention, then, is unobvious over the references of record.

Further, Andersen et al. provide no motivation to substitute the ester of Ahman et al. with a nitrile to arrive at the presently claimed compounds. "In determining the propriety of the Patent Office case for obviousness in the first instance, it is necessary

to ascertain whether or not the reference teachings would appear to be sufficient for one of ordinary skill in the relevant art having the reference before him to make the proposed substitution, combination, or other modification." *In re Linter*, 173 U.S.P.Q. 560, 562 (C.C.P.A. 1972). Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. *See In re Fine*, 5 U.S.P.Q.2d 1596 (Fed. Cir. 1988); *See also In re Jones*, 21 U.S.P.Q.2d 1941 (Fed. Cir. 1992).

The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *See In re Mills*, 16 U.S.P.Q.2d 1430 (Fed. Cir. 1990) Although the prior art may be capable of being modified to arrive at the claimed invention, there must be a suggestion or motivation in the reference to do so. *Id.* at 1432.

Ahman et al., the primary reference, shows an ester compound useful as an intermediate; however the reference does not specifically teach the claimed carboxylic acid isosteres. There is no disclosed use for the final products. The secondary reference provides no motivation to modify the primary reference to arrive at

the claimed invention.

Accordingly, Andersen et al. provide no motivation to one of ordinary skill in the art to modify Ahman et al. to arrive at the presently claimed compounds.

Claims 6-8 and 11 claim pharmaceutical compositions. Neither Ahman et al. nor Andersen in any way teach or suggest the use of the embodied compounds in pharmaceutical compositions. Accordingly, these claims are unobvious over the cited references.

Additionally, claims 14-25 claim methods of treating neurological disorders in an animal. Neither Ahman et al. nor Andersen in any way teach or suggest treating neurological disorders. Accordingly, these claims are unobvious over the cited references.

Accordingly, Andersen et al. provide no motivation to one of ordinary skill in the art to modify Ahman et al. to arrive at the presently claimed compounds.

C. Duffy, WO 92/21313

Duffy discloses a number of compounds having an ester attached at the 2-position of a central heterocyclic ring and an N-linked sulfonamide. An ester group is neither defined as nor included among the specific carboxylic acid isosteres recited in the presently claimed invention.

Andersen et al. do not remedy these deficiencies. Andersen et

al. (J. Med. Chem., 31, 417-425 (1996)) teach as stated above with respect to Ahman et al., the arguments of which are incorporated herein by reference.

Duffy, the primary reference, is directed to esters having immunosuppressive abilities and the reference does not teach the claimed carboxylic acid isosteres. Nowhere does Duffy state that the disclosed compounds have any neurotrophic abilities whatsoever. This disclosure, then, provides no disclosure teaching towards the present invention. The secondary reference, however, is directed to a different use and provides no motivation to modify the primary reference to arrive at the claimed invention.

Under the fact based inquiry of obviousness as stated by *In re Ochiai*, it is clear that it would not have been obvious to a person of ordinary skill in the art to modify the teachings of Duffy to arrive at the presently claimed invention for the reasons stated above with respect to Ahman et al. The claimed invention, then, is unobvious over the references of record.

Further, Andersen et al. provide no motivation to substitute the ester of Duffy with a nitrile to arrive at the presently claimed compounds. "In determining the propriety of the Patent Office case for obviousness in the first instance, it is necessary to ascertain whether or not the reference teachings would appear to be sufficient for one of ordinary skill in the relevant art having

the reference before him to make the proposed substitution, combination, or other modification." *In re Linter*, 173 U.S.P.Q. 560, 562 (C.C.P.A. 1972). Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. *See In re Fine*, 5 U.S.P.Q.2d 1596 (Fed. Cir. 1988); *See also In re Jones*, 21 U.S.P.Q.2d 1941 (Fed. Cir. 1992).

Additionally, the data and discussion provided by Andersen et al. show that the ester compounds do not possess the same activity as the nitrile compounds. The data provided on page 420 shows that the ester compounds possess a very low *in vivo* efficacy. The nitrile compounds, however, possess a much greater *in vivo* efficacy. Therefore, Andersen et al. do not teach equivalency but rather teach away from the present invention. *See In re Gurley*, 31 U.S.P.Q.2d 1130, 1131-1132 (Fed. Cir. 1994). Accordingly, a person of ordinary skill in the art would have been lead in a direction away from the present compounds and would not have expected the presently claimed compounds to possess the activity of the ester compounds of Duffy.

Accordingly, Andersen et al. provide no motivation to one of ordinary skill in the art to modify Duffy to arrive at the

presently claimed compounds.

Additionally, claims 14-25 claim methods of treating neurological disorders in an animal. Neither Duffy nor Andersen et al. in any way teach or suggest treating neurological disorders. Accordingly, these claims are unobvious over the cited references.

Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw the rejection of remaining claims 3-8, 11, and 14-27.

7. Rejection of Claims 1-4 under 35 U.S.C. § 112, 2d paragraph

The Official Action states that claims 1-4 are rejected under 35 U.S.C. § 112, second paragraph for the following reasons:

> Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
> It is unclear what is included in the claims because the definition of claims 1-4 included all possible compounds not yet been made i.e. carbocycle or heterocycle containing any combination of CH2, O, S or N in any chemical stable oxidation state, and such cycle can be optionally substituted in any position with R3. The meets and bounds of the claims can not be delineated. At the same time, the claims listed confusing provisos of many compounds. Applicants are urged to clearly claim what is the particular invention not what is not.

Claims 1 and 2 have been canceled, removing the present grounds for rejection as it applies to these claims.

Regarding the Examiner's assertion that claims 3 and 4 are indefinite for including all possible compounds which have "not yet been made", these claims are in compliance with the statute. It is

well established that an applicant need not disclose how to make every species within a genus in order to claim the genus; it is only necessary to show enough to enable one of ordinary skill in the art to practice the invention. *See In re Angstadt*, 190 USPQ 214 (C.C.P.A. 1976); *In re Wands*, 8 USQP2d 1400 (Fed. Cir. 1988).

Additionally, the sole requirement is that a broad claim be supported by an adequately broad disclosure. "The mere fact that a claim covers a large, or even an unlimited number of products, does not necessarily establish that it is too broad... It is not incumbent on an applicant...to demonstrate the operativeness of every substance falling within the scope of the broad claims to which he is entitled." *In re Sarett*, 140 USPQ 474, 486 (C.C.P.A. 1964). The present disclosure showing approximately 100 species falling within the scope of the present claims provides an adequately broad disclosure.

Regarding the Examiner's assertion that "the meets and bounds of the claims cannot be delineated", the scope of the property claimed by claims 3 and 4 is, in fact, definite. The purpose behind the definiteness requirement of 35 U.S.C. § 112, 2nd paragraph is to allow the public to know what is claimed and what is not since a patent grant gives a right to exclude others from making, using, selling, and importing the claimed invention.

For the present invention, others trying to not make, use,

sell, and import the invention (i.e. design around the invention) will predominantly be members of the pharmaceutical industry. These people have a very high degree of skill and are clearly capable of reading garden variety chemical claims to determine any possible infringement. A person of ordinary skill in the art would know whether or not a particular compound is covered by the claimed genus. Conversely, the provisoes clearly state what is not covered by the present claims. Applicants fail to understand the Examiner's statement that the metes and bounds of the claims cannot be delineated.

Furthermore, applicants have added new claims 72 and 81 which do not include the provisoes present in claims 3 and 4. These claims also clearly meet the definiteness requirement of 35 U.S.C. § 112, 2nd paragraph.

Regarding the Examiner's assertion that the negative provisoes included in claims 3 and 4 are improper, applicants remind the Examiner that there is nothing inherently ambiguous or uncertain about a negative limitation. The courts in both *In re Wakefield*, 164 U.S.P.Q. 636, 638 (C.C.P.A. 1970) and *In re Barr*, 170 U.S.P.Q. 330 (C.C.P.A. 1971) found claims containing negative limitations to be definite since each recited limitation was definite. Each recited proviso in claims 3 and 4 of the present application is definite. Accordingly, claims 3 and 4 meet the definiteness

requirement of 35 U.S.C. § 112, 2nd paragraph.

Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw the rejection of remaining claims 3-4.

8. Rejection of Claims 1-4 under 35 U.S.C. § 112, 1st paragraph

The Official Action states that claims 1-4 are rejected under 35 U.S.C. § 112, first paragraph for the following reasons:

> Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Please note that on one hand the scope of the claims are unclear yet at the same time many known compounds are excluded from the claims. For those compounds has yet to be made, the how to make and use rejection is applicable. For those compounds wherein the carboxylic acid isostere are those delineated in claims 3 and 4, no evidence has been provided that those "chemical isostere" all have "bioisostere" properties, since not all chemical isostere are biological isostere functionally (see Thornber).

Claims 1 and 2 have been canceled, removing the present grounds for rejection as it applies to these claims.

Applicants respectfully point out that no assertion was made by the Examiner regarding any deficiency in how to make the invention. The how to use prong of section 112 incorporates as a matter of law the requirement of 35 U.S.C. § 101 that the specification disclose as a matter of fact a practical utility for the invention. *In re Ziegler*, 992 F.2d 1197, 1200-01, 26 USPQ2d 1600, 1603 (Fed. Cir. 1993). Thus, the issues are limited as to

whether the instant claims enable a person of ordinary skill in the art to use the invention.

The test under 35 U.S.C. § 112, first paragraph, for determining compliance with the enablement requirement is whether one skilled in the art could make or use the claimed invention from the disclosures in the patent coupled with information known in the art without undue experimentation. *In re Brana*, 51 F.3d 1560, 1561 (Fed. Cir. 1995). Further, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must (emphasis in original) be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. *In re Langer*, 503 F.2d 1380, 1391 (CCPA 1974).

Applicants respectfully assert that the instant specification contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented. Applicants request the Examiner to withdraw her rejection and find the specification as in compliance with the enabling requirement of the first paragraph of § 112.

In re Langer and subsequent cases direct an Examiner to presume that a statement of utility made by an applicant is true. *See In re Brana*, 51 F.3d 1560, 1566 (Fed. Cir. 1995). When a statement of utility is evaluated, Patent Office personnel should begin their inquiry by asking if there is any reason to question the truth of the statement of utility. If the asserted utility is credible, a rejection based on lack of utility is inappropriate. If the applicant has presented facts that support the reasoning used in asserting a utility, Office personnel must present countervailing facts and reasoning sufficient to establish that a person of ordinary skill would not believe the applicant's assertion of utility. *Id.* (and as shown in USPTO Utility Examination Guidelines Sec. II, B, 2).

Both the case law and the Guidelines do not differentiate between § 101 and § 112 on this principle; they are unequivocal. Nonetheless, no discussion of credibility or the level of skill of persons of ordinary skill in the art were conducted, no well-reasoned statements clearly setting forth the reasoning were proffered, and no factual findings were relied upon (see Guidelines page 9, Sec. 3(a)); rather, a rejection was made instead.

Further, in order to make an enablement rejection, the Examiner has the initial burden to establish a *reasonable* basis to question the enablement provided for the claimed invention. *In re*

Wright, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

The Examiner's basis in this regard is deficient. The disclosure provides approximately 100 different specific embodiments of species falling within the present invention, as well as synthetic schemes, preferred pharmaceutical formulations, and data showing that the claimed compounds have been found to regrow both nerves and hair. A person of ordinary skill in the art would understand how to make and use the present invention based on the teachings present in the specification.

Regarding the Examiner's assertion that no evidence has been provided that chemical isostere's all have bioisostere properties, it is inconsistent for the Examiner to cite the Andersen and Thornber references in one rejection and simultaneously issue the present rejection. Applicants would appreciate clarification whether or not it is the Examiner's position that all bioisosteres are equivalent or not. These references both show that the term isostere is commonly used in the art. A person of ordinary skill in the art would understand the meaning of the term "carboxylic acid isostere" and what compounds are included by this term, especially in view of the specific carboxylic acid isosteres which are included in the claims and applicants very specific definition of the term in the specification.

Regarding the Examiner's assertion that the scope of claims 3

and 4 is unclear, the Examiner's attention is directed to the above arguments regarding the rejection under 35 U.S.C. § 112, 2nd paragraph, which remarks are hereby incorporated by reference. Accordingly, the scope of claims 3 and 4 is clear.

Accordingly, applicants respectfully request the Examiner to reconsider and withdraw the rejection of remaining claims 3-4.

9. Rejection of Claims 1-11 and 14-25 For Obviousness-Type Double Patenting

The Official Action states that claims 1-11 and 14-25 have been rejected for the following reasons:

> Claims 1-11, 14-25 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over patented claims of U.S. Patent No. 5,721,256 or 5,874,449. Although the conflicting claims are not identical, they are not patentably distinct from each other because broadly the instant claims embraced the patented claims in addition, the proviso limiting D is a chain is an prima facie obvious modification of knwon compounds since chain homologs are expected to have similar activity as the known compound. In re Lohr 137 USPQ 548; In re Hoke 195 USPQ 148; In re Fauque 1211 USPQ 425.

Claims 1, 2, and 9-10 have been canceled, removing the present grounds for rejection as it applies to these claims.

It should be noted that Applicants make the following arguments and comments based upon the claims as currently pending in this matter. As the prosecution of this application is not closed, such arguments and comments are made without prejudice to, or disclaimer of, any additional or different amendments,

arguments, or comments as may be offered during the continuing prosecution of this application, as well as any divisional filing(s) or continuation(s) of this application.

I. U.S. Patent No. 5,721,256

Applicants respectfully traverse the double patenting rejection over U.S. Patent No. 5,721,256, on the ground that the instant claims are patentable under both a one-way and a two-way obviousness determination.

Traversal: One-Way Obviousness Determination

Under a one-way obviousness determination, an obviousness-type double patenting rejection is improper where the application claims are patentably distinct from the prior patent claims.

A. The claimed subject matter

Applicants' claims as presently amended are directed to carboxylic acid and carboxylic acid isostere compounds, pharmaceutical compositions incorporating the same, and methods of using the same to treat a neurological disorder.

B. The claims of U.S. Patent No. 5,721,256

In contrast, 5,721,256 claims methods of using ester compounds to effect a neuronal activity.

C. The differences between the claimed subject matter and the claims of U.S. Patent No. 5,721,256

Claims 3-5 of the present application are compound claims.

None of the claims of the '256 patent are compound claims. Accordingly, present claims 3-5 are patentably distinct from the claims of the '256 patent.

Claims 6-8 and 11 of the present application are pharmaceutical composition claims. None of the claims of the '256 patent are pharmaceutical composition claims. Accordingly, present claims 3-5 are patentably distinct from the claims of the '256 patent.

Method claims 14-27 in the present application differ from the methods claimed in the '256 patent by requiring the use of carboxylic acid and carboxylic acid isostere compounds rather than ester compounds.

Contrary to the Office Action, the '256 patent does not contain claims having the present subject matter. The claims of the '256 patent are directed to methods of using ester compounds only. The present claims directed to methods of using carboxylic acids and carboxylic acid isosteres do not embrace the patented claims of the '256 patent. It would not have been obvious to modify the ester compounds of the '256 patent to arrive at the present inventive carboxylic acid and carboxylic acid isostere compounds.

Without any recitation in the claims of the '256 patent that the methods include the use of carboxylic acid and carboxylic

acid isostere compounds, the claims of the present application are unobvious over the claims of the '256 patent.

Traversal: Two-Way Obviousness Determination

Under a two-way obviousness determination, an obviousness-type double patenting rejection is improper if the application claims are patentably distinct from the prior patent claims, or the prior patent claims are patentably distinct from the application claims. If the application claims are not obvious variants of the prior patent claims, it is unnecessary to conduct the second prong of the test.

As stated above, the present claims are patentably distinct and unobvious from the claims of the '256 patent. Even if they are not, the claims of the '256 patent are patentably distinct and unobvious from the present claims.

The differences between U.S. Patent No. 5,721,256 and the claimed subject matter

The methods claimed in the '256 patent differ from the methods claimed in the present invention by reciting the use of ester compounds only. The claims of the '256 patent do not recite methods of using carboxylic acid or carboxylic acid isostere compounds. Consequently, the claims of the '256 patent are unobvious over the claims of the present application.

II. U.S. Patent No. 5,874,449

Applicants respectfully traverse the double patenting rejection over U.S. Patent No. 5,874,449, on the ground that the instant claims are patentable under both a one-way and a two-way obviousness determination.

Traversal: One-Way Obviousness Determination

Under a one-way obviousness determination, an obviousness-type double patenting rejection is improper where the application claims are patentably distinct from the prior patent claims.

A. The claimed subject matter

Applicants' claims as presently amended are directed to carboxylic acid and carboxylic acid isostere compounds, pharmaceutical compositions incorporating the same, and methods of using the same to treat a neurological disorder.

B. The claims of U.S. Patent No. 5,874,449

In contrast, 5,874,449 claims thioester compounds, pharmaceutical compositions incorporating the same, and methods of using the same to effect a neuronal activity.

C. The differences between the claimed subject matter and the claims of U.S. Patent No. 5,874,449

The claims of the present application differ from the claims in the '449 patent by requiring carboxylic acid and carboxylic acid isostere compounds rather than thioester compounds.

Contrary to the Office Action, the '449 patent does not

contain claims having the present subject matter. The claims of the '449 patent are directed to thioester compounds only. The present claims directed to carboxylic acids and carboxylic acid isosteres do not embrace the patented claims of the '449 patent. It would not have been obvious to modify the thioester compounds of the '449 patent to arrive at the present inventive carboxylic acid and carboxylic acid isostere compounds.

Without any recitation in the claims of the '449 patent that carboxylic acid and carboxylic acid isostere compounds are included, the claims of the present application are unobvious over the claims of the '449 patent.

Traversal: Two-Way Obviousness Determination

Under a two-way obviousness determination, an obviousness-type double patenting rejection is improper if the application claims are patentably distinct from the prior patent claims, or the prior patent claims are patentably distinct from the application claims. If the application claims are not obvious variants of the prior patent claims, it is unnecessary to conduct the second prong of the test.

As stated above, the present claims are patentably distinct and unobvious from the claims of the '449 patent. Even if they are not, the claims of the '449 patent are patentably distinct and unobvious from the present claims.

The differences between U.S. Patent No. 5,874,449 and the claimed subject matter

The '449 patent claims differ from the present claims by reciting thioester compounds only. The claims of the '449 patent do not recite carboxylic acid or carboxylic acid isostere compounds. Consequently, the claims of the '449 patent are unobvious over the claims of the present application.

Accordingly, applicants respectfully request the Examiner to reconsider and withdraw the rejection of remaining claims 3-8, 11, and 14-27.

10. Rejection of Claims 1-11 and 14-25 under 35 U.S.C. § 103(a)

The Official Action states that claims 1-11 and 14-25 are provisionally rejected under 35 U.S.C. § 103(a) as being unpatentable over the corresponding US pending application of WO 99/10340.

As the basis of this rejection, the Official Action states:

> Claims 1-11, 14-25 are provisionally rejected under 35 U.S.C. 103(a) as being unpatentable over the corresponding US pending application of WO 99/10340. Applicants attention is drawn to that the US pending application corresponding to the WO 99/10340 patent generically claims the instant compounds for the same use. The proviso limitation disclaimed certain species but does not obviated the generic scope as encompassed by the 99/10340 patent.
> This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicants respectfully traverse this rejection. Applicants

are uncertain whether the present rejection is a statutory rejection under 35 U.S.C. 103(a) or a rejection under the judicially created doctrine of obviousness-type double patenting. The Examiner's remarks are unclear in this regard.

If the present rejection is under 35 U.S.C. 103(a), applicants believe this is an improper rejection. Under MPEP § 706.02(k), "where two applications of different inventive entities are copending and the filing dates differ, a provisional rejection under 35 U.S.C. 102(e)/103 should be made in the later filed application if the applications have a common assignee or a common inventor. Otherwise the confidential status of applications under 35 U.S.C. 122 must be maintained." The cited reference has neither a common assignee nor a common inventor with the present application. Accordingly, the rejection is improper for violating the confidential status of applications under 35 U.S.C. 122.

Additionally, 35 U.S.C. 103 (a) states that "A patent may not be obtained...if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." (Emphasis added) Here, the cited reference is not yet a piece of the prior art. Since

U.S. patent applications are maintained in secrecy until a patent is granted, applicants are presently unable to obtain a copy of the U.S. application corresponding to WO 99/10340. The Examiner is respectfully requested to either provide applicants with the file history for the cited U.S. application or withdraw the present rejection.

If the present rejection is under the judicially created doctrine of obviousness-type double patenting, applicants believe this is an improper rejection. Under MPEP § 804, a provisional double patenting rejection is proper only between two applications having either a common inventive entity or a common assignee. Neither case applies here.

Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw the rejection of remaining claims 3-8, 11, and 14-27.

CONCLUSION

Based upon the above remarks, the presently claimed subject matter is believed to be novel and patentably distinguishable over the prior art of record. The Examiner is therefore respectfully requested to reconsider and withdraw the rejections of the remaining claims and allow all pending claims 3-8, 11, 14-27, and 72-89 presented herein for reconsideration. Favorable action with an early allowance of the claims pending in this

application is earnestly solicited.

The Examiner is welcomed to telephone the undersigned attorney if he has any questions or comments.

Respectfully submitted,
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